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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,025	10/19/2006	Dennis L. Panicali	701281	3646

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ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

Office Action Summary	Application No.	Applicant(s)	
	10/579,025	PANICALI ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-10,12 and 16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10,12 and 16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :06/28/2010; 11/03/2010; and 11/18/2010.

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/28/2010 has been entered.

Claims 2-6, 11, 13-15, and 23-44 are cancelled. Claims 1 and 12 are amended. Claims 1, 7-10, 12 and 16-22 are pending.

Claims 1, 7-10, 12 and 16-22 are currently under examination to the extent of the following elected species: an orthopox virus vector as recited in claim 7; MUC-1 as recited in claim 12; and MVA as recited in claim 20

This application 10/579,025 filed on 10/19/2006 is a 371 of PCT/US2004/038643 filed on 11/12/2004 which claims benefit of 60/519,354 filed on 11/12/2003.

Claim Objections

1. Previous objection of claim 1 for recitation of "(c) at regular intervals thereafter administering at least a second poxvirus vector containing a one or more DNA segments" is **withdrawn** because the claim has been amended with "a" deleted.

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

2. Previous rejection of claims 1, 7-10, 12 and 16-22 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **withdrawn** because claim 1 has been amended.

Amended claim 1 filed on 06/28/2010 reads as follows: A method for inducing an immunological response against a malignant pancreatic cell in an individual, said wherein the method comprises (a) selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) carcinoembryonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigen portion thereof or a wobbled version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) carcinoembrvonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigenic portion thereof or a wobbled version thereof, such that an immunological response against the malignant pancreatic cell is induced in the individual.

Amended claim 1 filed on 06/28/2010 no longer recites the limitation "or a modified version therefore".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1, 7-10, 12, and 16-22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over **Laidlaw et al.** (U.S. patent 7,273,605, issued date 09/25/2007, effective filing date 11/30/2001) in view of **Pecher** (WO 01/24832, PCT/DE00/03443, filed on 09/26/2000; this document is cited as reference AA in the IDS filed by Applicant on 07/09/2008), and **Kotera et al.** (Kotera et al., Humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients. Cancer Res. 54(11):2856-60, 1994). Applicant's arguments filed 06/28/2010 have been fully considered and they are not persuasive. Previous rejection of claim 13 is moot because claim 13 has been cancelled. Previous rejection is **maintained** for the reasons of record advanced on pages 4-14 of the office action mailed on 12/28/2009.

For the clarity and completeness of this office action, the rejection for the reasons of record advanced on pages 4-14 of the office action mailed on 12/28/2010, is reiterated below with revisions addressing claim amendments filed on 06/28/2010.

Amended claim 1 filed on 06/28/2010 reads as follows: A method for inducing an immunological response against a malignant pancreatic cell in an individual, said wherein the method comprises (a) selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) carcinoembryonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigen portion thereof or a wobbled version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) carcinoembrvonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigenic portion thereof or a wobbled

version thereof, such that an immunological response against the malignant pancreatic cell is induced in the individual.

Claims 7-10 and 17-21 further limit to specified orthopox vector and avipox vector for expression of carcinoembryonic antigen (CEA) and mucin (MUC). Claims 12 and 16 further limit the recited mucin (MUC), various recited mucins (MUCs). Claim 22 further limits to recited set interval for administration.

Claim interpretations: The limitation "wobbled version thereof" recited in claim 1 and the limitation "wobbled MUC-1" recited in claim 16 are interpreted as identical MUC-1 polypeptide sequences encoded by different genetic codes due to codon degeneration (i.e. a given amino acid can be encoded by multiple codons that are different in the third nucleotide of a given codon in a MUC-1 mRNA molecules recognized by tRNA molecules during translation.

Laidlaw et al. teaches a method which comprises administering a priming composition (which comprises a first non-replicating viral vector) and a boosting composition (which comprises a second non-replicating viral vector) to a subject to treat and/or prevent a cancer. Laidlaw et al. teaches a viral particle comprising such a genome and its use to deliver a nucleotide of interest (NOI) to a target cell, and a fowlpox virus genome which has modifications in one or more wild-type FPV genes (See abstract, lines 5-10 of column 2, lines 57-60 of column 13, Laidlaw et al.).

With regard to the limitations pertaining to poxvirus, orthopox virus, avipox vector, and MVA recited in claims 7-10, and 17-21 of instant application, Laidlaw et al. teaches poxviruses have been exploited as recombinant vectors for the heterologous expression of foreign proteins. In particular, recombinant vaccinia virus has been studied as a tool for transient expression of genes in mammalian cells and an experimental recombinant vaccine vector (See lines 17-22,

column 1, Laidlaw et al.). Laidlaw et al. teaches the family of poxviruses can be split into two subfamilies, the Chordopoxvirinae and the Entomopoxviriniae. The Chordopoxvirinae (poxviruses of vertebrates) include geni of orthopoxviruses and avipoxviruses. In a preferred embodiment the present invention provides a vaccine, priming or boosting composition which comprises a non-replicating pox virus vector. (See lines 41-50, column 6, Table 2, Laidlaw et al.). Laidlaw et al. teaches that concern about the capacity of vaccinia virus to replicate in mammalian cells has limited its clinical use and led to the search for safer alternatives, and these include attenuated vaccinia viruses, such as modified vaccinia Ankara (MVA) (See lines 38-41, column 1, Laidlaw et al.).

With regard to the limitation orthopox vector is administered before the avipox vector is administered recited in claim 21, Laidlaw et al. teaches that the two viral vectors maybe derived from viruses belonging to the same family (such as pox viruses) but different geni (e.g. the genus of orthopoxviruses and the genus of avipoxviruses) (See lines 40-47, column 7, Laidlaw et al.).

With regard to the limitation the limitation the set interval is 20 days to 90 days, recited in claim 22, Laidlaw et al. teaches various prime-boost immunization regimes using different poxvirus vectors, such as 3-4 weeks intervals (See Example 14, columns 31-32, Laidlaw et al.).

With regard to carcinoembryonic antigen (CEA), mucin (MUC) as tumor associated antigens, Laidlaw et al. teaches nucleotide of interest (NOI) may, for example, be or encode one of the following: an antigen, cytokines, immune co-stimulatory molecules, immunomodulatory molecules. In one preferred embodiment, the NOI is capable of encoding a disease (e.g. cancer) associated antigen. Exposure to an antigen in the context of a fowlpox vector may provoke or

boost immune responses to the antigen such that an existing or subsequent challenge is dealt with more effectively. (See lines 37-53, column 13, Laidlaw et al.). Laidlaw et al. teaches the target antigen may be an antigen which is recognized by the immune system after infection with the disease; and for cancers, preferred colon cancer antigens: **CEA**, MUC-1, MAGE-12, mutant P53 whereas preferred breast cancer antigens are **MUC-1**, HER2, CEA (See lines 19-30, column 20, Laidlaw et al.). Laidlaw et al. teaches number of other compositions may be employed in heterologous vaccination programs. If the genome/particle of the present invention comprises an NOI (optionally capable of encoding a POI, protein of interest), then preferably the other composition comprises the same NOI or POI. Other compositions, in addition to pox virus vectors, include "naked DNA", non-viral vector systems and other viral vector systems, and naked DNA (or RNA) may be linear or circular (for example, a plasmid). (See lines 48-57, column 14, Laidlaw et al.). Furthermore, related to immunization with two antigens, Laidlaw et al. teaches immunization of C57BL/6 mice using pSG2.ME1 and/or FP9.ME1 elicited IFNγ-secreting T cells against the LCMV epitopes ($H\text{-}2^b$), but not against the tumour epitopes ($H\text{-}2^b$) (FIGS. 17A-17B). The total frequency of IFNγ-secreting T cells elicited against LCMV epitopes by prime/boost immunization with pSG2.ME1/FP9.ME1 was significantly higher than that elicited by homologous immunisation with FP9.ME1 (P w 0.003) alone or pSG2.ME 1 (P=0.016) alone (See lines 60-67, column 46, Laidlaw et al.).

Laidlaw et al. does not explicitly teach a first and a second vector containing one or more DNA segments that encode (i) carcinoembryonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigen portion thereof or a wobbled version thereof for inducing immunological response against a malignant pancreatic cell.

Pecher teaches a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and/or the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system. The pharmaceutical composition is provided comprising a plasmid which contains the gene for the human carcinoembryonic antigen (CEA) SEQ No. 2., and another plasmid which contains the human mucin gene MUC1, active fragments thereof or at least 3 repeats of amino acid sequence SEQ No. 1, which reads on wobble MUC-1 or wobbled mini-MUC recited in claim 16 of instant application (See abstract, Pecher, W/O 01/24832, 2000). It is noted that Laidlaw et al. teaches that a number of other compositions may be employed in heterologous vaccination programs. If the genome/particle of the present invention comprises an NOI (optionally capable of encoding a POI), then preferably the other composition comprises the same NOI or POI. Other compositions include "naked DNA", non-viral vector systems and other viral vector systems (See lines 48-54, column 14, Laidlaw et al.).

Kotera et al. teaches humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients.

Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Laidlaw et al. regarding a method which comprises administering a priming composition (which comprises a first non-replicating viral vector) and a boosting composition (which comprises a second non-replicating viral vector) to a subject to treat and/or prevent a cancer; a viral particle comprising such a genome and its use to deliver a nucleotide of interest (NOI) to a target cell, and a poxvirus vector or a plasmid for

expression of NOI; and both CEA and MUC-1 being preferred colon cancer antigens as well as breast cancer antigens, with (i) the teachings of Pecher regarding the pharmaceutical composition is provided comprising a plasmid which expresses tumor antigen carcinoembryonic antigen (CEA) and/or the tumor antigen mucin, active fragments thereof, and (ii) the teachings of Kotera et al. regarding humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients, to arrive at the claimed methods recited in claims 1, 7-10, 12, and 16-22 of instant application for inducing an immunological response against a malignant pancreatic cell in an individual, comprising the recited steps.

One having ordinary skill in the art would have been motivated to combine the teachings of Laidlaw et al., Pecher, and Kotera et al. because (i) Pecher explicitly teaches a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system against breast and colon cancer cells, (ii) Laidlaw et al. teaches a poxvirus vector or a plasmid vector for the expression of CEA and MUC-1, which are established tumor associated antigens (TAAs) for colon and breast cancers, and (iii) Kotera et al. teaches humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from pancreatic, colon, and breast cancer patients.

There would have been a reasonable expectation of success given (i) successful establishment of various prime-boost immunization regimes for clinical trials using combination of poxvirus vectors each expresses a NOI, which encodes a polypeptide or an antigenic determinant that induces immunological response in an individual, and CEA and MUC-1 are preferred tumor associated antigens for immunization against breast and colon cancer cells, by

the teachings of Laidlaw et al., (ii) a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and express the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system, and the pharmaceutical composition comprising a plasmid expressing the tumor antigen carcinoembryonic antigen (CEA, SEQ ID No:2) and the tumor antigen mucin (MUC1), by the teachings of Pecher, and (iii) humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients, by the teachings of Kotera et al.

Thus, the claimed invention as a whole was clearly prima facie obvious.

Applicant's arguments

Applicant argues that the Laidlaw reference does not disclose that CEA or MUC are pancreatic tumor antigens, or the administration of a first and second vector each containing a DNA segment encoding CEA and MUC to produce an immunological response against a malignant pancreatic cell, as required by the pending claims (See Applicant's remarks filed on 06/28/2010).

The deficiencies of the Laidlaw reference are not remedied by the Pecher or Kotera references.

The Pecher reference indicates that CEA and/or MUC-1 are expressed by human tumors and not by one vector, as required by the pending claims. Specifically, the Pecher reference discloses a pharmaceutical composition comprising one vector (e.g., a plasmid) comprising the gene encoding MUC-1 and/or another vector (e.g., a plasmid) comprising the gene encoding CEA. Thus, CEA and MUC-1 are not in the same vector as required by the pending claims. Additionally, the Pecher reference does not identify CEA and/or MUC-1 as pancreatic tumor antigens, or disclose the administration of a first and a second vector containing a DNA segment encoding CEA and MUC-1 to produce an immunological response against a malignant

pancreatic cell, as required by the pending claims.

While the Kotera reference identifies a tandem repeat epitope of human MUC-1 in sera from pancreatic cancer patients, the Kotera reference does not disclose a vector encoding MUC-1, much less a first and second vector containing a DNA segment encoding CEA and MUC-1, or the administration of the vectors to produce an immunological response against a malignant pancreatic cell, as required by the pending claims. Furthermore, the Kotera reference does not disclose that CEA is a pancreatic tumor antigen.

Thus, none of the cited references, when considered alone or in combination, teach or suggest inducing an immunological response against a malignant pancreatic cell by administering a first poxvirus vector containing one or more DNA segments that encode (i) CEA or an antigen portion thereof and (ii) MUC or an antigen portion thereof or a wobbled version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) CEA or an antigen portion thereof and (ii) MUC or an antigenic portion thereof or a wobbled version thereof, as required by the claims (See Applicant's remarks filed on 06/28/2010).

As discussed in the previous Reply to Office Action, the inventive methods result in unexpected benefits, which further evidence the nonobviousness of the present invention, as defined by the pending claims, over the combination of the disclosures of the cited references. In particular, the inventive methods result in the beneficial effect of stimulating the immune system to target against the CEA and MUC-1 antigens, which are found on over 90% of pancreatic tumor cells (see, e.g., Example 11 of the specification). As a result, metastatic pancreatic cancer patients receiving this vaccine were shown to have a trend toward an overall survival greater than the expected median overall survival (see Abstract of Schuetz et al., J. Clin. Oncol., 2005 ASCO Annual Meeting Proceedings, 23 (16S Part I of II in June 1 Supplement): 2576 (2005); submitted herewith).

Applicant states that the benefits attendant the present invention are unexpected and surprising in view of the teachings in the art at the earliest priority date of the application. As evidenced by Palmowski et al. (J. Immunol., 168:4391-4398 (2002); submitted herewith) and Brody et al. (Immunol., 22:75-85 (1972); submitted herewith), prior to the invention, the presentation of two antigens together (at the same location) was thought to result in competition

between the two antigens with one antigen being dominant, thereby resulting in a reduced immune response to one or both of the antigens (see, e.g., page 4397, second column, fourth full paragraph, of Palmoski et al., and page 83, lines 1-3, of Brody et al.).

Applicant states that for these reasons, the subject matter of the pending clams would not have been obvious to one of ordinary skill in the art at the relevant time in view of the combined disclosures of the Laidlaw, Pecher, and Kotera references. Accordingly, Applicant states that the obviousness rejection should be withdrawn.

Response to Applicant's arguments

The Examiner would like to direct Applicant's attention to recent decision by U.S. Supreme Court in KSR International Co. v. Teleflex, Inc. that forecloses the argument that a **specific** teaching, suggestion, or motivation is an absolute requirement to support a finding of obviousness. See recent Board decision Ex parte Smith, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1936) [available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf; and KSR Guidelines Update has been published in the Federal Register at 75 Fed. Reg. 53643-60 (Sep. 1, 2010) and is posted at USPTO's internet Web site at http://www.uspto.gov/patents/law/notices/2010.jsp]. The Examiner notes that in the instant case, even in the absence of recent decision by U.S. Supreme Court in KSR International Co. v. Teleflex, Inc., the suggestion and motivation to combine Laidlaw et al., Pecher, and Kotera et al. has been clearly set forth above in this office action.

It is noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

As indicated above and responded previously, Applicant is reminded that the claimed method as a whole was clearly prima facie obvious based on the collective teachings of Laidlaw et al., Pecher, and Kotera et al., not based on individual reference viewed separately. The claimed method as a whole was clearly prima facie obvious because (i) Pecher explicitly teaches a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and the tumor antigen mucin, and to the use

thereof as a vaccine in humans for activating the immune system against breast and colon cancer cells, (ii) Laidlaw et al. teaches a poxvirus vector or a plasmid vector for the expression of CEA and MUC-1, which are established tumor associated antigens (TAAs) for colon and breast cancers, and (iii) Kotera et al. teaches humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from pancreatic, colon, and breast cancer patients.

As responded previously, it is noted that the teachings by Pecher regarding "a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and/or the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system" certainly reads on "a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system". Furthermore, related to immunization with two antigens, Laidlaw et al. teaches immunization of C57BL/6 mice using pSG2.ME1 and/or FP9.ME1 elicited IFNγ-secreting T cells against the LCMV epitopes (H-2^b), but not against the tumour epitopes (H-2^b) (FIGS. 17A-17B). The total frequency of IFNγ-secreting T cells elicited against LCMV epitopes by prime/boost immunization with pSG2.ME1/FP9.ME1 was significantly higher than that elicited by homologous immunization with FP9.ME1 (P w 0.003) alone or pSG2.ME 1 (P=0.016) alone (See lines 60-67, column 46, Laidlaw et al.).

With regard to the argument "the Kotera reference does not disclose that CEA is a pancreatic tumor antigen", the arguments have been fully considered and found not persuasive.

It is noted that Kotera et al. specifically teaches humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from pancreatic, colon, and breast cancer patients whereas Laidlaw et al. teaches a poxvirus vector or a plasmid vector for the expression of CEA and MUC-1, which are established tumor associated antigens (TAAs) for colon and breast cancers. The presence of CEA and MUC-1 as tumor associated antigens (TAAs) in colon and breast cancers taught by Laidlaw et al. and the presence of MUC-1 as tumor associated antigens (TAAs) in pancreatic, colon, and breast cancer taught by Kotera et al. certainly suggest the possibility the presence of CEA as tumor associated antigens (TAAs) in as tumor associated antigens (TAAs) in pancreatic cancer. Furthermore, it is worth noting that the claimed methods

for "inducing an immunological response against a malignant pancreatic cell in an individual" do not require any specific limitations regarding the "immunological response" elicited by the expression of CEA versus the "immunological response" elicited by the expression of MUC-1. Based on the combined teachings of Laidlaw, Pecher, and Kotera, a skilled artisan would, at least, observe humoral immunity (i.e. production of antibody) against a tandem repeat epitope of human mucin MUC-1 in sera from pancreatic patient, which is certainly encompassed by the claimed methods. Additionally, at the time of filing of instant application, it was known in the art that expression of CEA leads to the induction of CEA-specific T-cell immune response (i.e. cellular immunity) (See for instance, **Aarts et al.**,Vector-based vaccine/cytokine combination therapy to enhance induction of immune responses to a self-antigen and antitumor activity, Cancer Res. 62(20):5770-7, 2002; this reference has been cited as non-patent literature C1 in the IDS filed by Applicant on 05/11/2006).

Applicant's arguments that "metastatic pancreatic cancer patients receiving this vaccine were shown to have a trend toward an overall survival greater than the expected median overall survival" have been fully considered and found not persuasive because the claimed methods only require "an immunological response against the malignant pancreatic cell is induced in the individual".

The Examiner acknowledges the teachings of the references by Palmowski et al. (J. Immunol. 168:4391-4398 (2002); submitted by Applicant on 06/28/2010) and Brody et al. (Immunol. 22:75-85 (1972); submitted by Applicant on 06/28/2010) regarding "antigenic competition". Brody et al. (1972) taught that immunization of an animal with two or more antigens, simultaneously or within a relatively brief time span, frequently results in a diminution of the immune response to one or more of these antigens as compared with control animals immunized with only a single antigen. Brody et al. (1972) further taught that antigenic competition does not occur if the two antigens are injected so as to drain into different groups of regional lymph nodes. This is true even if a 3- or 7-day time interval is imposed between injection of the two antigens. Bearing the teachings of Brody et al. (1972) in mind, nevertheless, the "antigenic competition" does not negate simultaneous administration of multiple antigens for immunization purpose. In this regard, for instance, administration of combined vaccine of measles, mumps, and rubella (MMP) for children has been practiced for many countries,

including US, for decades [See, Section 2 immunogenicity, page 2111-2117, **Wellington et al.,** Measles, mumps, rubella vaccine (Priorix; GSK-MMR): a review of its use in the prevention of measles, mumps and rubella. Drugs 63(19):2107-26, 2003]. Furthermore, it is worth noting again that the claimed methods for "inducing an immunological response against a malignant pancreatic cell in an individual" do not require any specific limitations regarding the "immunological response" elicited by the expression of CEA versus the "immunological response" elicited by the expression of MUC-1.

With regard to the teachings of Palmowski et al. (2002), the Examiner notes that Palmowski et al. specifically investigated "competition between CTL narrows the immune response induced by prime-boost vaccination protocols" (See title and abstract, Palmowski et al., 2002), which is focused on "competition between CTL" [i.e. competition within a subset of cellular immunity mediated by **c**ytotoxic **T**-**l**ymphocytes (CTL, killer T cells)]. However, as discussed in the preceding paragraphs and in the maintained 103(a) rejection, Kotera, et al. specifically teaches humoral immunity (i.e. pertaining to production of antibody) against a tandem repeat epitope of human mucin MUC-1 in sera from pancreatic patient whereas it was known in the art that expression of CEA leads to the induction of CEA-specific T-cell immune response (i.e. pertaining to cellular immunity). Therefore, Applicant's arguments that "prior to the invention, the presentation of two antigens together (at the same location) was thought to result in competition between the two antigens with one antigen being dominant, thereby resulting in a reduced immune response to one or both of the antigens" have been fully considered and found not persuasive.

It is further noted that at the time of filing of instant application, simultaneous expression of multiple antigens from a DNA vector-based vaccine for induction of antitumor immune response was known in the art. For instance, Aarts et al. specifically described recombinant poxvirus, the rVand fowlpox viruses, containing the human CEA gene and the murine B7-1, ICAM-1, and LFA-3 genes (designated rV-CEA/TRICOM and rF-CEA/TRICOM, respectively) (See Materials and Methods, page 5771, **Aarts et al.,**Vector-based vaccine/cytokine combination therapy to enhance induction of immune responses to a self-antigen and antitumor activity, Cancer Res. 62(20):5770-7, 2002; this reference has been cited as non-patent literature C1 in the IDS filed by Applicant on 05/11/2006).

Conclusion

4. No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/
Primary Examiner
Art Unit 1632